

DETAILED ACTION

1. Amendment and response filed by applicants dated Dec. 20, 2007 have been entered and considered carefully.

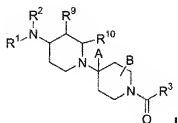
Claims 1-20, 31-40 have been canceled. Claims 21-30 are pending.

2. *Examiner's Amendment*

Authorization for this examiner's amendment was given in a telephone interview with Dr. Krishna G. Banetjee on Mar. 18, 2008.

In claim 21, the scope of R² is limited to those of example 2, p.50-63.

21. (Currently amended) A compound represented by the structural formula I



or a pharmaceutically acceptable salt or solvate thereof; wherein:

R¹ is



R² is [aryalkyl] benzyl or 4-fluorobenzyl;

R³ is selected from the group consisting of 6-membered heteroaryl, and 6-membered heteroaryl-N-oxide, wherein said 6-membered heteroaryl or heteroaryl-N-oxide is pyrimidine or pyrimidine-N-oxide respectively, each of which is optionally substituted with 1-4 substituents which can be the same or different and are independently selected from the group consisting of R¹¹, R¹², R¹³, R¹⁴ and R¹⁵;

R⁴ is 1-3 substituents selected from the group consisting of H, halo, alkyl, haloalkyl, alkoxy, cycloalkyl, amide, CF₃, OCF₃, aryl, heteroaryl, -XR¹, -CN, -CO₂H,

-CO₂R²², R⁸-aryl(C₁-C₆)alkyl-, R⁸-heteroaryl(C₁-C₆)alkyl-, -C(O)NR²¹R²², -C(O)NH₂, wherein R⁴ can be the same or different and is independently selected when there is more than one R⁴ present;

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R⁷ is selected from the group consisting of aryl substituted aryl, heteroaryl, alkyl, haloalkyl and cycloalkyl;

R⁸ is 1, 2 or 3 substituents selected from the group consisting of H, halo, (C₁-C₆)alkyl, (C₁-C₆)alkoxy, -CF₃, -OCF₃, CH₃C(O)-, -CN-, CH₃SO₂-, CF₃SO₂- and -NH₂, wherein R⁸ can be the same or different and is independently selected when there are more than one R⁸ present;

R⁹, R¹⁰ and B can be the same or different and are each independently selected from the group consisting of hydrogen, (C₁-C₆)alkyl, and -(C₁-C₆)heteroalkyl;

R¹¹ and R¹² can be the same or different and are each independently selected from the group consisting of -(C₁-C₆)alkyl, -(C₁-C₆)haloalkyl, halogen, -NR¹⁹R²⁶ -OH, CF₃-, OCH₃-, O-acyl, and -OCF₃;

R¹³ is selected from the group consisting of hydrogen, R¹¹, H, phenyl, NO₂-, -CN-, -CH₂F, -CHF₂-, -CHO, -CH=NOR¹⁹, pyridyl-N-oxide, pyrimidinyl, pyrazinyl, N(R²⁰)CO N R²⁰R²¹-, -NHCONH (chloro-(C₁-C₆)alkyl) -, -NHCONH ((C₃-C₁₀)-cycloalkyl(C₁-C₆)alkyl), -NHCO(C₁-C₆)alkyl, -NHCOCF₃-, -NHCOCF₃-, -NHSO₂N((C₁-C₆)alkyl, -NHSO₂(C₁-C₆)alkyl, -N(SO₂CF₃)₂-, -NHSO₂(C₁-C₆)alkyl, (C₃-C₁₀)cycloalkyl, -SR²², -SOR²²-, -SO₂R²²-, -SO₂N H(C₁-C₆)alkyl, -OSO₂(C₁-C₆)alkyl, -OSO₂CF₃-, hydroxy(C₁-C₆)alkyl, -CONR¹⁹R²⁰-, -CON (CH₂CH₂-O -CH₃)₂-, -OCONH(C₁-C₆)alkyl, -CO₂R¹⁹, Si(CH₃)₃ and -B(OC(CH₃)₂)₂;

R¹⁴ is selected from the group consisting of (C₁-C₆)alkyl, -(C₁-C₆)haloalkyl -NH₂ and R¹⁵-phenyl;

R¹⁵ is 1-3 substituents selected from the group consisting of hydrogen, (C₁-C₆)alkyl, (C₁-C₆)haloalkyl, -CF₃-, -CO₂R²⁰-, -CN, (C₁-C₆)alkoxy and halogen; wherein R¹⁵ can be the same or different and is independently selected when there are more than one R¹⁵ present;

R¹⁹, R²⁰ and R²¹ can each be the same or different and are each independently selected from the group consisting of H, (C₁-C₆)alkyl and (C₃-C₆)cycloalkyl;

R²² is selected from the group consisting of -(C₁-C₆)alkyl, -(C₁-C₆)haloalkyl, -(C₂-C₆)hydroxyalkyl, (C₂-C₆)alkylene, (C₃-C₆)cycloalkyl, aryl and aryl(C₁-C₆)alkyl-;

A is selected from the group consisting of H, (C₁-C₆)alkyl, and (C₂-C₆)alkenyl,

M is aryl optionally substituted with R⁴; and

X is selected from the group consisting of CH₂, SO₂, SO, S, and O, with the following proviso: when R¹ is phenyl-, or naphthyl, R² cannot be H, (C₁-C₆)alkyl or -C(O)- (C₁-C₆)alkyl.

There are duplicate claims 28-29. The **first set** claims 28-29 are canceled.

3. Reason for Allowance

The following is an examiner's statement of reasons for allowance:

Applicants have provided evidence that in Table 2 of the Declaration filed on Mar. 8, 2007, the comparison between example 72 and the reference compound of the prior art showed that the dimethylpyrimidyl compounds and dimethylphenyl compounds of the prior art do have similar activity for which an prima facie obviousness was established in the office action. However, example 9, which showed that when R² is benzyl such compounds have unexpected property in that it has reduced plasma protein binding thus higher efficiency in vivo (see p.4-5 declaration). Applicants have also limited the claims to the compounds commensurate to this unexpected result that is R² being benzyl or fluorobenzyl as disclosed in example 2 (p.50-63). Claims 21-30 as currently amended are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*OACS/Chang
Mar. 24, 2008*

*/Celia Chang/
Primary Examiner
Art Unit 1625*